Listing of Claims.

Please amend the claims as shown below by deleting the material indicated by strike-through and adding the underlined material. This listing of claims will replace all prior versions and listings of the claims in this application.

1. (Currently amended) A propagation-defective adenovirus vector comprising ~~an~~ a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein ~~comprising one or more deletion(s) in one or more region(s) selected from the group consisting of:~~

~~(a) the 100K region, wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said deleted region,~~

~~(b) the IVa2 region, wherein said deletion(s) essentially prevents the expression of a functional IVa2 protein from said deleted region, and~~

~~(c) the preterminal protein region, wherein said deletion(s) essentially prevents the expression of a functional preterminal protein from said deleted region~~.

2. (Currently amended) The adenovirus of Claim 1, wherein said adenovirus can be propagated in a transcomplementing cell ~~that transcomplements said deletion(s) in said adenovirus genome~~.

3. (Original) The adenovirus of Claim 1, wherein said adenovirus can be propagated in a transcomplementing cell in the absence of a helper.

4. (Currently amended) The adenovirus of Claim 1, wherein said adenovirus genome further lacks an E1 region or comprises an E1 region comprising one or more deletion(s) therein ~~in the E1 region~~.

5. (Currently amended) The adenovirus of Claim 1, wherein said adenovirus genome further lacks an E3 region or comprises an E3 region comprising one or more deletion(s) therein ~~in the E3 region~~.

Claims 6-12. (Cancelled)

13. (Currently amended) The adenovirus of Claim 1 ~~12~~, wherein said adenovirus genome comprises a 100K region comprising ~~deletion(s) comprises~~ a deletion ~~in the 100K region~~ at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

14. (Canceled)

15. (Currently amended) The adenovirus of Claim 4 ~~14~~, wherein said adenovirus is disclosed herein as [E1$^-$, 100K$^-$]Ad.

16. (Original) The adenovirus of Claim 15, wherein said adenovirus comprises one or more heterologous nucleotide sequences.

Claims 17 -24. (Cancelled)

25. (Original) The adenovirus of Claim 1 further comprising one or more heterologous nucleotide sequences.

26. (Original) The adenovirus of Claim 25, wherein said heterologous nucleotide sequence(s) is operatively associated with expression control sequences.

27. (Original) The adenovirus of Claim 26, wherein said expression control sequences include a promoter.

28. (Original) The adenovirus of Claim 27, wherein said promoter is selected from the group consisting of liver-specific, muscle-specific, and brain-specific promoters.

29. (Original) The adenovirus of Claim 27, wherein said promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1-α promoter, PγK promoter, MFG promoter, and Rous sarcoma virus promoter.

30. (Currently amended) The adenovirus of Claim 25, wherein said adenovirus genome further comprises ~~5' and 3' adenovirus inverted terminal repeat sequences, an adenovirus packaging sequence, and~~ an adenovirus E1A enhancer sequence.

31. (Original) The adenovirus of Claim 25, wherein said heterologous nucleotide sequence(s) encodes a protein or peptide.

32. (Original) The adenovirus of Claim 31, wherein said protein or peptide is a therapeutic protein or peptide.

33. (Original) The adenovirus of Claim 31, wherein said protein or peptide is an immunogenic protein or peptide.

34. (Original) The adenovirus of Claim 31, wherein said protein or peptide is a reporter protein or peptide.

35. (Currently amended) The adenovirus of Claim 31, wherein said heterologous nucleotide sequence(s) encodes an antisense nucleotide sequence or non-translated RNA.

36. (Original) The adenovirus of Claim 31, wherein said protein or peptide is a lysosomal protein.

37. (Original) The adenovirus of Claim 31, wherein said protein or peptide is associated with a metabolic disorder.

38. (Original) The adenovirus of Claim 37, wherein said protein or peptide is associated with a lysosomal storage disease.

39. (Original) The adenovirus of Claim 38, wherein said protein or peptide is selected from the group consisting of β-galactosidase, β-hexosaminidase A, β-hexosaminidase B, GM_2 activator protein, glucocerebrosidase, arylsulfatase A, galactosylceramidase, acid sphingomyelinase, acid ceramidase, acid lipase, α-L-iduronidase, iduronate sulfatase, heparan N-sulfatase, α-N-acetylglucosaminidase acetyl-CoA, glucosaminide acetyltransferase, N-acetylglucosamine-6-sulfatase, arylsulfatase B, β-glucuronidase, α-mannosidase, β-mannosidase, α-L-fucosidase, N-aspartyl-β-glucosaminidase, α-neuraminidase, lysosomal protective protein, α-N-acetyl-galactosaminidase, N-acetylglucosamine-1-phosphotransferase, cystine transport protein, sialic acid transport protein, the CLN3 gene product, palmitoyl-protein thioesterase, saposin A, saposin B, saposin C, and saposin D.

40. (Original) The adenovirus of Claim 37, wherein said protein or peptide is associated with a glycogen storage disease.

41. (Original) The adenovirus of Claim 40, wherein said protein or peptide is selected from the group consisting of glucose 6-phosphatase, lysosomal acid α glucosidase, glycogen debranching enzyme, branching enzyme, muscle phosphorylase, liver phosphorylase, phosphorylase kinase, muscle phosphofructokinase, glycogen synthase, phosphoglucoisomerase, muscle phosphoglycerate kinase, phosphoglycerate mutase, and lactate dehydrogenase.

Claims 42-43. (Cancelled)

44. (Withdrawn) A propagation-defective adenovirus vector comprising ~~an~~ a recombinant adenovirus genome that ~~comprising~~:

(a) lacks a coding sequences for ~~one or more deletions in the E1 region, wherein said deletion(s) essentially prevents the expression of~~ one or more functional E1 proteins ~~from said deleted region~~, and

(b) lacks a coding sequence for ~~one or more deletions in the polymerase region, wherein said deletion(s) essentially prevents the expression of~~ a functional polymerase protein ~~from said deleted region~~.

Claims 45-49. (Cancelled)

50. (Withdrawn) The adenovirus of Claim 44, wherein said adenovirus genome further lacks a 100K region or comprises a 100 K region comprising one or more deletions therein ~~in the 100K region~~.

Claim 51. (Cancelled)

52. (Withdrawn) The adenovirus of Claim 44, wherein said adenovirus genome further lacks a preterminal protein region or comprises a preterminal protein

region comprising one or more deletions therein ~~in the preterminal protein region.~~

Claims 53. (Cancelled)

54. (Withdrawn) The adenovirus of Claim 52, wherein said adenovirus genome further (a) lacks an E3 region or comprises an E3 region comprising one or more deletions therein ~~in the E3 region~~ and also (b) lacks a 100K region or comprises a 100K region comprising one or more deletions therein ~~in the 100K region~~.

55. (Withdrawn) The adenovirus of Claim 54 ~~52~~, wherein said adenovirus genome further lacks a IVa2 region or comprises a IVa2 region comprising one or more deletions therein ~~in the E3 region, one or more deletions in the IVa2 region, and one or more deletions in the 100K region~~.

Claims 56-58. (Cancelled)

59. (Currently amended) A propagation-defective adenovirus vector comprising ~~an~~ a recombinant adenovirus genome that lacks a functional coding sequence for a 100K protein and comprises ~~comprising~~ a heterologous nucleotide sequence encoding a lysosomal acid α-glucosidase ~~and one or more deletions in one or more regions selected from the group consisting of:~~

~~(a) the polymerase region, wherein said deletion(s) essentially prevents the expression of a functional polymerase from said deleted region,~~

~~(b) the preterminal protein region, wherein said deletion(s) essentially prevents the expression of a functional preterminal protein from said deleted region,~~

~~(c) the 100K region, wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said deleted region; and~~

~~(d) the IVa2 region, wherein said deletion(s) essentially prevents the expression of a functional IVa2 protein from said deleted region~~.

60. (Withdrawn) The adenovirus of Claim 59, wherein said adenovirus genome comprises a polymerase region comprising a deletion ~~in the polymerase region~~ at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

61. (Withdrawn) The adenovirus of Claim 59, wherein said adenovirus comprises a preterminal protein region comprising a deletion ~~in the preterminal protein region~~ at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

62. (Withdrawn) The adenovirus of Claim 59, wherein said adenovirus genome (a) lacks a polymerase region or comprises a polymerase region comprising one or more deletions therein ~~in the polymerase region~~ and (b) lacks a preterminal protein region or comprises a preterminal protein region comprising one or more deletions therein ~~in the preterminal protein region~~.

63. (Withdrawn) The adenovirus of Claim 59, wherein said heterologous nucleotide sequence is operatively associated with a promoter.

64. (Withdrawn) The adenovirus of Claim 63, wherein said promoter is selected from the group consisting of liver-specific and muscle-specific promoters.

65. (Withdrawn) The adenovirus of Claim 63, wherein said promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1-α promoter, PγK promoter, MFG promoter, and Rous sarcoma virus promoter.

66. (Currently amended) The adenovirus of Claim 59, wherein said protein or peptide is human lysosomal acid α-glucosidase ~~adenovirus is selected from the group consisting of AdhGAAΔpol, Ad/EF1-α/hGAAΔpol, Adh5'sGAAΔpol, Ad/EF1-α/h5'sGAAΔpol, AdhGAAΔpp, Ad/EF1-α/hGAAΔpp, Adh5'sGAAΔpp, Ad/EF1-α/h5'sGAAΔpp~~.

67. (Currently amended) The adenovirus of Claim 59, wherein said adenovirus genome comprises a 100K region comprising a deletion ~~in the 100K region~~ at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

68. (Currently amended) The adenovirus of Claim 59, wherein said adenovirus genome comprises a IVa2 region comprising a deletion ~~in the adenovirus IVa2 region~~ at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or a corresponding region of adenoviruses of other serotypes.

69. (Currently amended) A mammalian cell comprising the adenovirus of Claim 1.

70. (Original) The cell of Claim 69, wherein said adenovirus comprises one or more heterologous nucleotide sequences encoding a protein or peptide.

Claims 71-74. (Cancelled)

75. (Currently amended) A mammalian cell comprising the adenovirus of Claim 59.

Claims 76-79. (Cancelled)

80. (Currently amended) An isolated mammalian cell comprising an isolated DNA comprising a nucleotide sequence encoding an adenovirus 100K protein ~~The cell of Claim 78~~, wherein said cell can propagate an adenovirus genome that essentially lacks expression of a functional 100K protein.

81. (Currently amended) The cell of Claim 80 ~~78~~, wherein said nucleotide sequence is stably integrated into the genome of the ~~packaging~~ cell.

82. (Original) The cell of Claim 81, wherein said cell is a K-16 cell.

83. (Currently amended) The cell of Claim 80 ~~78~~, wherein said nucleotide sequence further encodes a constitutive promoter that is operatively associated with the sequence encoding said adenovirus 100K protein.

84. (Original) The cell of Claim 83, wherein said cell is a C7 cell constitutively expressing the 100K protein.

85. (Currently amended) The cell of Claim 80 ~~78~~, wherein said nucleotide sequence encodes an inducible promoter that is operatively associated with the sequence encoding said adenovirus 100K protein.

86. (Currently amended) The cell of Claim 80 ~~78~~, further comprising ~~an~~ a recombinant adenovirus genome, wherein said adenovirus genome lacks a coding sequence for a functional 100K protein ~~comprises one or more~~

~~deletion(s) in the 100K region, and further wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said 100K region~~.

Claims 87-93. (Cancelled)

94. (Currently amended) An isolated DNA ~~of Claim 93, wherein said isolated DNA comprises an~~ comprising a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein ~~comprising the nucleotide sequence encoding the deleted adenovirus 100K protein~~.

95. (Currently amended) The isolated DNA of Claim 94, wherein said adenovirus genome comprises a ~~deletion(s) in the~~ 100K region comprising ~~comprises~~ a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

96. (Original) A vector comprising the isolated DNA of Claim 94.

97. (Original) The vector of Claim 96, wherein said vector is a plasmid.

98. (Original) The vector of Claim 97, wherein said vector is disclosed herein as pcDNA3+100K.

Claims 99-104 (Cancelled)

105. (Currently amended) A method of producing a propagation-defective adenovirus vector ~~particle comprising one or more deletion(s) in the adenovirus genome~~, comprising:

introducing ~~an~~ a propagation-defective adenovirus into a mammalian cell, wherein the introduced adenovirus comprises ~~an~~ a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein ~~comprising one or more deletions in one or more regions selected from the group consisting of:~~

~~(a) the 100K region, wherein the deletion(s) essentially prevents the expression of a functional 100K protein from the deleted region,~~

~~(b) the IVa2 region, wherein the deletion(s) essentially prevents the expression of a functional IVa2 protein from the deleted region, and~~

~~(c) and the preterminal protein region, wherein the deletion(s) essentially prevents the expression of a functional preterminal protein from the deleted region~~;

wherein the mammalian cell expresses a functional 100K protein and transcomplements the function(s) lacking ~~deleted~~ from the adenovirus genome; and

collecting the propagation-defective adenovirus vector ~~particle~~.

106. (Original) The method of Claim 105, wherein the collected adenovirus has a titer of at least 100 infectious units per cell.

107. (Currently amended) The method of Claim 105, wherein the adenovirus genome further lacks and E1 region or comprises an E1 region comprising one or more deletion(s) therein ~~in the E1 region and the mammalian cell further transcomplements the deletion(s)~~.

108. (Currently amended) The method of Claim 105, wherein the adenovirus genome further lacks an E3 region or comprises an E3 region comprising one or more deletion(s) therein ~~in the E3 region~~.

109. (Withdrawn) The method of Claim 105, wherein the adenovirus genome further lacks a polymerase region or comprises a polymerase region comprising one or more deletion(s) therein ~~in the polymerase region and the mammalian cell further transcomplements the deletion~~.

110. (Cancelled)

111. (Currently amended) The method of Claim 105 ~~110~~, wherein the adenovirus genome comprises a ~~deletion(s) in the~~ 100K region comprising ~~comprises~~ a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

112. (Currently amended) The method of Claim 111, wherein the ~~introduced~~ adenovirus is disclosed herein as [$E1^-$, $100K^-$]Ad.

113. (Currently amended) The method of Claim 105 ~~110~~, wherein the mammalian cell comprises a nucleotide sequence encoding a functional 100K protein stably integrated into the genome of the mammalian cell.

114. (Original) The method of Claim 113, wherein the mammalian cell is a K-16 cell.

115. (Currently amended) The method of Claim 113 ~~110~~, wherein the mammalian cell constitutively expresses the functional 100K protein.

116. (Original) The method of Claim 115, wherein the mammalian cell is a C7 cell constitutively expressing the 100K protein.

Claims 117-131 (Cancelled)

132. (Original) The method of Claim 105, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.

133. (Currently amended) A composition comprising a plurality of the propagation-defective adenovirus vector ~~particle~~ produced by the method of Claim 105.

Claims 134-145 (Cancelled)

146. (Currently amended) A method of producing a propagation-defective adenovirus vector ~~particle~~, comprising:

introducing a bacterial plasmid comprising ~~an~~ a recombinant adenovirus genome into a bacterial cell, wherein said adenovirus genome lacks a coding sequence for a functional 100K protein ~~comprises one or more deletions in one or more regions from the group consisting of:~~

~~(a) the polymerase region, wherein said deletion(s) essentially prevents the expression of a functional polymerase from said deleted region,~~

~~(b) the preterminal protein region, wherein said deletion(s) essentially prevents the expression of a functional preterminal protein from said deleted region,~~

~~(c) the 100K region, wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said deleted region, and~~

~~(d) the IVa2 region, wherein said deletion(s) essentially prevents the expression of a functional IVa2 protein from said deleted region~~;

amplifying the bacterial plasmid in the bacterial cell;

recovering the amplified bacterial plasmid from the bacterial cell;

linearizing the recovered bacterial plasmid;

introducing the linearized plasmid into a mammalian cell that transcomplements the deleted functions in the adenovirus genome; and

collecting the propagation-defective adenovirus vector ~~particle~~.

147. (Original) The method of Claim 146, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.

148. (Original) The method of Claim 147, wherein the heterologous nucleotide sequence(s) encodes a lysosomal acid α-glucosidase.

Claims 149-206 (Cancelled)

207. (Currently amended) A method of producing a gutted adenovirus containing a minichromosome, comprising:

introducing into a mammalian cell expressing a functional 100K protein:

a plasmid comprising an adenovirus inverted terminal repeat (ITR), an adenovirus packaging sequence, and a heterologous nucleotide sequence, and

a helper adenovirus comprising ~~an~~ a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein ~~comprising one or more deletions in the adenovirus 100K region, wherein the deletion(s) prevents the expression of a functional protein from the deleted region~~;

collecting the gutted adenovirus containing the minichromosome from the mammalian cell.

208. (Currently amended) The method of Claim 207, wherein the adenovirus genome comprises a ~~deletion(s) in the~~ 100K region comprising ~~comprises~~ a

deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a homologous region adenoviruses of other serotypes.

209. (Currently amended) The method of Claim 207, wherein the ~~introduced~~ helper adenovirus is disclosed herein as [E1$^-$, 100K$^-$]Ad.

210. (Withdrawn) The method of Claim 207, wherein the adenovirus genome further lacks a coding sequence for a functional IVa2 protein ~~one or more deletions in the IVa2 region~~ and the mammalian cell expresses a functional IVa2 protein.

211. (Withdrawn) The method of Claim 207, wherein the adenovirus genome further lacks a coding sequence for a functional polymerase protein ~~comprises one or more deletions in the polymerase region~~ and the mammalian cell expresses a functional polymerase protein.

212. (Withdrawn) The method of Claim 207, wherein the adenovirus genome further lacks a coding sequence for a functional preterminal protein ~~comprises one or more deletions in the preterminal protein region~~ and the mammalian cell expresses a functional preterminal protein.

213. (Original) The method of Claim 207, wherein the nucleotide sequence encoding the functional 100K protein is stably integrated into the genome of the mammalian cell.

214. (Original) The method of Claim 213, wherein the mammalian cell is a K-16 cell.

215. (Original) The method of Claim 207, wherein the mammalian cell constitutively expresses the functional 100K protein.

216. (Original) The method of Claim 215, wherein said mammalian cell is a C7 cell constitutively expressing the 100K protein.

217. (Original) The method of Claim 207, wherein the helper adenovirus lacks a packaging sequence.

218. (Original) The method of Claim 207, wherein the helper adenovirus has a modified packaging signal that does not promote the encapsidation of the helper plasmid.

219. (Currently amended) The method of Claim 207, wherein the helper adenovirus further comprises lox sites flanking the packaging sequence and the mammalian cell produces the cre recombinase ~~recombinanse~~ protein.

220. (Original) A method of delivering a nucleotide sequence into a cell comprising introducing into the cell a composition comprising a plurality of the gutted adenovirus particles of Claim 207.

221. (Original) The method of Claim 220, wherein said introducing is carried out *in vivo*.

222. (Original) The method of Claim 207, further comprising the step of separating the gutted adenovirus from contaminating helper adenovirus.

Claims 223-236 (Cancelled)